

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



REC'D 11 OCT 2004

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Applicant's or agent's file reference SCB 762PCT	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP 03/03923	International filing date (day/month/year) 15.04.2003	Priority date (day/month/year) 23.04.2002
International Patent Classification (IPC) or both national classification and IPC C07C49/693		
Applicant INDENA S.P.A. et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
- I ☒ Basis of the opinion
  - II ☐ Priority
  - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - IV ☐ Lack of unity of invention
  - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI ☐ Certain documents cited
  - VII ☐ Certain defects in the international application
  - VIII ☐ Certain observations on the international application

Date of submission of the demand  12.11.2003	Date of completion of this report  08.10.2004
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Breimaier, W  Telephone No. +49 89 2399-8327  

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/EP 03/03923**

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-13 as originally filed

**Claims, Numbers**

1-7 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims	1-7
	No: Claims	
Inventive step (IS)	Yes: Claims	1-7
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-7
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP 03/03923

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

D1 : WO 99/64388

D2 : WO 99/41220

The present invention concerns compounds of general formula (I) which are said to possess anti-depressant, anxiolytic and anti-neurodegenerative activities according to claims 1 to 7.

**novelty**

The subject-matter according to claims 1 to 7 is novel pursuant to Art. 33(2) PCT.

D1 describes OH-functionalized (ad)hyperforin derivatives of general formula (I) as an anti-depressant (see pages 5 and 6 and the claims).

D2 describes stable (ad)hyperforin salts of general formula (I) which are useful as anti-depressants and for treating eg Alzheimer's disease (see page 6, tables II-IV and claims).

None of the documents of the available prior art describes the 8-halogen substituted derivatives of (ad)hyperforin of general formula (I) according to claim 1.

Thus, novelty for the subject-matter according to claims 1 to 7 is given.

**inventive step**

The subject-matter according to claims 1 to 7 is inventive pursuant to Art. 33(3) PCT.

In view of the closest state of the art D1 and D2, the problem posed is the provision of further stable (ad)hyperforin derivatives which possess anti-depressant and anti-neurodegenerative activities.

The above problem is solved by (ad)hyperforin derivatives which are substituted at the 8-position with halogen according to claim 1. The results reported on page 8 show that the halogenated compounds of the invention possess the desired activities. In particular, the compounds as claimed are more active than the parent hyperforin.

In the absence of any indication in the available prior art that substitution of (ad)hyperforin with halogen at the 8-position would furnish the corresponding stable derivatives with the desired activity, an inventive step is acknowledged.